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REGIONAL CUTANEOUS MICROVASCULAR FLOW RESPONSES DURING GRAVITATIONAL AND LBNP STRESSES

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INTRODUCTION

The most significant cardiovascular event during the transition to microgravity is the redistribution of vascular transmural pressures that results from the loss of hydrostatic gradients along the length of the body. The well-documented effects of this redistribution include facial venous engorgement, headache, and a significant decrease in leg volume [7]. These effects predominantly represent bulk fluid volume shifts, especially in the venous macro- and microcirculation, where volume is a direct function of pressure, related by the mechanical compliance of the vascular compartment.

When considering the effect of gravitational pressure alterations on *microcirculatory* blood flow and volume, however, this direct monotonic relationship no longer applies. Regional microvascular perfusion is largely a function of local arteriolar tone, which is subject to a variety of central and local controls. Lower body venous pooling during application of footward gravitational stress unloads arterial and cardiopulmonary baroreceptors, increasing sympathetic arteriolar tone to elicit vasoconstriction and a general decrease in microvascular perfusion. The same stimulus also triggers an increase in the levels of circulating vasoactive hormones, such as norepinephrine and angiotensin II, further augmenting arteriolar tone. Vasomotor tone is also mediated by local mechanisms such as myogenic autoregulation [5] and veno-arteriolar reflexes [3], which enhance microvascular tone in response to elevated local arteriolar and venular pressure, respectively.

Due to the regional variability of local hydrostatic pressures, microvascular flow responses to gravitational stress probably vary along the length of the body. Although these differences in local autoregulation have been observed previously during whole-body tilting [1], they have not been investigated during application of artificial gravitational stresses, such as lower body negative pressure (LBNP) or $+G_z$ centrifugation. Although these stresses can create equivalent G-levels at the feet [2], they result in distinct distributions of vascular transmural pressure along the length of the body, and should consequently elicit different magnitudes and distributions of microvascular response. In the present study, the effects of whole-body tilting and LBNP on the level and distribution of microvascular flows within skin along the length of the body were compared.

METHODS

Informed consent was obtained from 9 (5M, 4F) healthy subjects, age 23-48. Subjects refrained from caffeine and alcohol for 24h prior to data collection. Cutaneous blood flow was measured at the lateral neck, anterior femoral and tibial crest regions, using three laser Doppler flowmeters (Model BPM403A, Vasamedics Inc., St. Paul, MN). Flowmeter outputs were digitized continuously using a microcomputer-based data acquisition system. For head-up tilt (HUT) experiments, subjects were initially placed supine on an electric motorized tilt table. For negative pressure sessions, subjects were placed supine into the LBNP chamber and sealed at the superior iliac crest. In both cases, subjects opposed the footward force against a footplate. On random days, subjects underwent either the following stepwise tilting or LBNP protocol:

Time (min)	G_z at feet	Tilt Angle	LBNP (mmHg)
0:00	(0.0)	0°	0
1:00	(0.2)	12°	20
1:40	(0.4)	24°	40
2:20	(0.6)	37°	60
3:00	(0.8)	53°	80
3:40	(1.0)	90°	100
4:20	(0.8)	53°	80
5:00	(0.6)	37°	60
5:40	(0.4)	24°	40
6:20	(0.2)	12°	20
7:00	(0.0)	0°	0

Both protocols ended with 5 min of supine recovery. Room temperature was regulated at 23±0.5°C.

For each subject, flowmeter outputs were averaged over the last 10s of each stress interval. ANOVA with post-hoc *t*-tests on raw flowmeter data were used to determine significant differences ($p<0.05$) between responses. For presentation, flowmeter signals are normalized to the mean level present at initial supine baseline. Means and standard errors are reported.

RESULTS

Normalized microvascular flows during HUT and LBNP are shown in Figure 1. Microvascular flow at the level of the neck increased significantly during HUT, but not during LBNP. Microvascular flows in the lower leg and thigh were reduced significantly during low levels of each stress and remained so up to 90° HUT at both measurement sites and up to 100 mmHg LBNP in the thigh. From 40 to 100 mmHg LBNP, flow in the lower leg increased significantly from 35.0±5.6% of baseline to 75.0±13.6% at 100 mmHg LBNP, and abruptly fell to 34.7±6.6% on the return to 80 mmHg. Throughout the HUT protocol, relative flow in the lower leg was significantly lower than in the thigh. This was not the case during LBNP.

During HUT, average heart rate increased from 61.2±3.5 beat/min (bpm) to 76.1±3.5 bpm at 90° HUT and returned to 57.9±3.7 bpm following 5 min supine recovery. During LBNP, heart rate increased from 74.1±4.7 bpm to 100.8±6.9 bpm at 100 mmHg LBNP, and returned to 64.8±5.2 bpm after 5 min recovery.

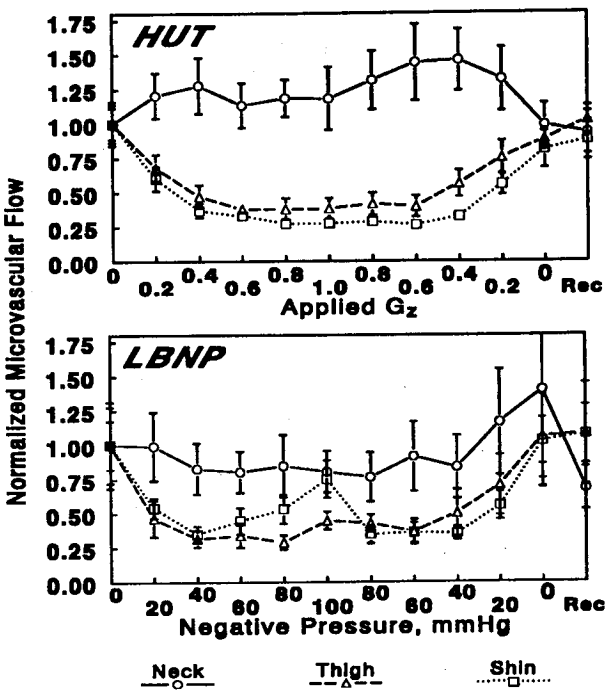

Figure 1. Relative levels of cutaneous microvascular blood flow at the neck, thigh, and shin during HUT (top, n=7) and LBNP (bottom, n=6). Four subjects are common between the two groups. Bars denote standard errors.

DISCUSSION

Our results demonstrate that microvascular responses to gravitational stress vary significantly along the length of the body, and suggest that local autoregulation plays an important role in these reactions. Upright standing posture and 100 mmHg LBNP are approximately equivalent in terms of vascular transmural pressures at foot level [2]. However, LBNP exerts an abrupt and uniform increase in transmural pressure over the lower body, in contrast to the linearly increasing pressure profile present during upright posture. Furthermore, the change in neck microvascular pressure with LBNP depends mostly on systemic regulation of mean arterial pressure, in contrast to the known hydrostatic decrease that occurs with upright posture. Due to the importance of autoregulatory reactions to local pressure, we hypothesize that HUT and LBNP differ with respect to both the magnitude and distribution of microvascular flows.

During whole-body tilting, regional changes in microvascular flow generally oppose changes in local vascular transmural pressures. During the transition to upright posture, flow increases in the upper body and decreases in the lower body, with the lower leg (the site of the greatest postural pressure increase) exhibiting the greatest flow reduction. Low levels of LBNP elicit similar vasoconstrictor responses at both leg measurement sites, while flow at the neck does not change significantly. These responses are in accordance with the hypothesized vascular transmural pressures which occur with the different stresses.

In the lower body, at the capillary level, there exists an important qualitative distinction between HUT and LBNP. Due to viscous dissipation in the arterioles, increased hydrostatic pressure during upright posture is not fully realized in the capillary networks [6]. In contrast, the stress of LBNP is transmitted equally to all sections of the microvasculature. The flow increase observed in the lower leg during high levels of LBNP could therefore represent enhanced capillary recruitment due to mechanical microvascular distension. Although microvascular flow at this site during 100 mmHg LBNP did not exceed baseline levels, this recruitment effect was apparently sufficient to offset partially the flow-reducing effect of upstream vasoconstriction. Furthermore, enhanced capillary recruitment represents a significant increase in surface area for microcirculatory transport, and may therefore accelerate edema formation in the lower body during high levels of LBNP.

Although the importance of the cutaneous microcirculation in volume regulation during gravitational stress is not well understood [4], the regulatory mechanisms discussed here are not unique to skin. Consequently, the responses observed here are probably also representative of what occurs in deeper, less accessible tissues, such as skeletal muscle. The results of the present study demonstrate that LBNP differs significantly from upright posture at the microvascular level. This distinction is potentially crucial when considering LBNP as an alternative orthostatic stress for use as a cardiovascular countermeasure for long-duration space flight. For example, external compression may be necessary during LBNP to provide a gradient of transmural blood pressures similar to upright standing posture [2].

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